ANSWER TO PHOTO QUIZ (PAGE 415)

ITCHING DERMATITIS ON THE LEG OF A 46-YEAR-OLD HIV-POSITIVE MAN FROM JAMAICA

DIAGNOSIS

The differential diagnosis of the skin lesions was malignant syphilis (also known as lues maligna or ulceronodular syphilis), tertiary gummatous syphilis or an endemic treponematose. Histopathology showed an interstitial lymphohistiocytic infiltrate with formation of non-necrotizing granulomas. Giemsa, Ziehl-Neelsen and Grocott stainings were negative. The culture showed no growth of mycobacteria and fungi. During follow-up, the RPR increased to 1:256. The polymerase chain reaction (PCR) test for *treponema pallidum* conducted on the skin biopsy was positive. A Treponema IgG immunoblot was performed and all bands were positive. Combined with the rise of the RPR titer, this confirmed the diagnosis of an active syphilis infection.

Malignant syphilis is a rare form of secondary syphilis often accompanied with the prodromal phase of fever, headache and myalgia.[1,2] The first systematic studies of malignant syphilis were performed by Haslund[3] and Neisser[4], who differentiated malignant syphilis as a severe form of secondary syphilis from the gummas of tertiary syphilis. The following diagnostic criteria for malignant syphilis are defined as: strongly positive RPR titer, a severe Jarisch-Herxheimer reaction, characteristic macroscopic and microscopic morphology and rapid resolution of the lesions with antibiotics.[5] The macroscopic characteristics are pleomorphic papulopustules, beginning ulcerations and deep ulcerations covered with crusts. The microscopic characteristics are an interstitial lymphohistiocytic and plasma cell-rich infiltrate with formation of non-necrotizing granulomas, sometimes in the presence of spirochetes. We diagnosed our patient with malignant syphilis because of the lamellar crusting, multiple ulcers, strongly positive RPR titer, a positive *treponema pallidum* PCR test of suspected syphilis lesions and rapid resolution of the lesions after antibiotic treatment.[2]

Although tertiary gummatous syphilis was considered as a differential diagnosis, we consider this less likely in our patient. Lamellar crusting is not a feature of tertiary syphilis and gummatous disease generally takes years to decades to develop after initial infection, although progression may occur faster in HIV-positive patients.[6]

In our patient, neurosyphilis was excluded with a cerebrospinal fluid examination and cardiovascular syphilis was excluded with an ultrasound of the heart.

Endemic treponematoses consisting of *Treponema pallidum* subsp *pertenue* (yaws), *T. pallidum* subsp *endemicum* (bejel), and *T. carateum* (pinta) were also considered as differential diagnoses. It is very difficult to distinguish venereal syphilis from the endemic treponematoses by serology only. However, yaws and bejel were less likely due to the patient's country of origin and travel history. Pinta can be present in the Americas, including the Caribbean, but primary skin lesions due to pinta do not ulcerate. Furthermore, the rapid resolution of the lesions after treatment is not typical for pinta.

Penicillin is the best treatment for malignant syphilis: 10 to 14 days of IV treatment[7-10], as well as 2.4 MIU intramuscularly, weekly for three weeks[11-13], have shown good response. Malignant syphilis is considered as form of secondary syphilis, so with a confirmed infection within one year, a single dose of 2.4 MIU penicillin could also be considered. In our patient, neurosyphilis was not present, but the duration of infection and previous treatments were not documented. Therefore, we treated the patient with benzathin benzylpenicillin, 2.4 MIU intramuscularly for three consecutive weeks. The lesions disappeared completely in the following weeks leaving only hyperpigmentation.

In conclusion, atypical skin disorders in a patient with syphilis may be a form of malignant syphilis, especially in a HIV co-infected patient. The characteristic macroscopic and microscopic morphology, strongly positive RPR titer and rapid resolution of the lesions with antibiotics may lead to this rare diagnosis.

REFERENCES

1. Tucker JD, Shah S, Jarell AD, Tsai KY, Zembowicz A, Kroshinsky D. Lues maligna in early HIV infection case report and review of the literature. Sex Transm Dis. 2009;36:512-4.
2. Kumar B, Muralidhar S. Malignant syphilis: a review. AIDS Patient Care STDS. 1998;12:921-5.
3. Haslund A. Syphilis maligna. Archiv fur Dermatologie und Syphilis. 1897;38:345-92.
4. Neisser A. Malignant syphilis. Br J Dermatol. 1897;9:11-26.
5. Fisher DA, Chang LW, Tuffanelli DL. Lues maligna. Presentation of a case and a review of the literature. Arch Dermatol. 1969;99:70-3.
6. Colmegna I, Koehler JW, Garry RF, Espinoza LR. Musculoskeletal and autoimmune manifestations of HIV, syphilis and tuberculosis. Curr Opin Rheumatol. 2006;18:88-95.
7. Pariser H. Precocious noduloulcerative cutaneous syphilis. Arch Dermatol. 1975;111:76-7.
8. Balachandran C, Sabita L, Kantharaj GR. Perforation of hard palate in lues maligna associated with HIV infection. Genitourin Med. 1997;73:225.
9. Sands M, Markus A. Lues maligna or ulceronodular syphilis in a man infected with human immunodeficiency virus: case report and review. Clin Infect Dis. 1995;20:387-90.
10. Wappner D, Carbia S, Gioseffi L, et al. Malignant Syphilis. Clin Infect Dis. 1997;25:1343.
11. Don PC, Rubinstein R, Christie S. Malignant syphilis (lues maligna) and concurrent infection with HIV. Int J Dermatol. 1995;34:403-7.
12. Held JL, Ross M, Beltrani V, et al. Noduloulcerative or "malignant" syphilis occurring in an otherwise healthy woman: report and review of a dramatic dermatosis. Cutis. 1990;45:119-22.
13. Ficarra G, Zaragoza AM, Stendardi L, et al. Early oral presentation of lues maligna in a patient with HIV infection. A case report. Oral Surg Oral Med Oral Pathol. 1993;75:728-32.